Citation:

Schulze MB, Liu S, Rimm EB, Manson JE, Willett WC, Hu FB. Glycemic index, glycemic load, and dietary fiber intake and incidence of type 2 diabetes in younger and middle-aged women. *Am J Clin Nutr*. 2004 Aug; 80(2): 348-356.

PubMed ID: 15277155

Study Design:

Prospective Cohort Study

Class:

B - Click here for explanation of classification scheme.

Research Design and Implementation Rating:

POSITIVE: See Research Design and Implementation Criteria Checklist below.

Research Purpose:

To examine the associations of glycemic index (GI) and load (GL) and different sources of dietary fiber with incidence of type 2 diabetes in a group of younger women.

Inclusion Criteria:

A member of the Nurses' Health Study II.

Exclusion Criteria:

- Did not complete a dietary questionnaire in 1991 or if more than nine items on it were left blank
- Reported total energy intake was implausible (less than 500 or more than 3,500kcal per day)
- History of diabetes, cancer (except non-melanoma skin cancer), or cardiovascular disease reported on either the 1989 or 1991 questionnaire
- No data on physical activity in 1991.

Description of Study Protocol:

Recruitment

Subjects were members of the Nurses' Health Study II, a prospective cohort study (started in 1989) of female nurses in the US who were age 24 to 44 years at study initiation.

Design

Prospective cohort with follow-up questionnaires administered every two years

Dietary Intake/Dietary Assessment Methodology

133-food item semiquantitative food-frequency questionnaire (FFQ): Women were asked how often on average they had consumed specified amounts of foods over the previous year.

Statistical Analysis

- Cox proportional hazards regression analysis was used stratified on five-year age categories to estimate relative risks for each category of intake compared to the lowest category. Subjects diagnosed with diabetes or who died during follow-up were censored at the date of diagnosis or death. Dietary measurements made after diagnosis of cancer (except non-melanoma skin cancer) or cardiovascular disease were not used due to potential disease-related dietary modifications
- Linear trends across categories of dietary intake was tested by assigning each participant the median value for the category and modeling this value as a continuous variable
- Effect modification by body mass index (BMI), physical activity and family history of diabetes was tested by performing analyses stratified by these variables and by evaluating interaction terms.

Data Collection Summary:

Timing of Measurements

- Dietary measurements by questionnaire occurred in 1991 and 1995
- New diagnoses of diabetes, age, weight, smoking status, contraceptive use, post-menopausal hormone replacement therapy (HRT), history of high blood pressure and history of high blood cholesterol were assessed with biennial questionnaires
- Physical activity was assessed in 1991 and 1997
- Family history of diabetes and height were assessed in 1989.

Dependent Variables

Type 2 diabetes: Women who reported a new diagnosis of diabetes (except gestational diabetes) on any biennial questionnaire were sent supplementary questionnaires to confirm the diagnosis. Confirmation required at least one of the following:

- An elevated plasma glucose concentration plus at least one classic symptom of diabetes
- No symptoms, but at least two elevated plasma glucose concentrations on different occasions
- Treatment with a hypoglycemic medication.

Independent Variables

- Average dietary glycemic index: Sum of the products of the carbohydrate content per serving for each food item times the number of servings of that food per day, times its glycemic index and divided by the total daily carbohydrate intake
- Glycemic load: Amount of carbohydrates multiplied by the average glycemic index
- Total daily carbohydrate intake as a percent of total energy
- Total daily fiber, cereal fiber, fruit fiber and vegetable fiber intake.

Control Variables

- BMI
- Total calorie intake
- Alcohol intake

- Physical activity
- Family history of diabetes
- Smoking history of high blood pressure
- History of high blood cholesterol
- Post-menopausal hormone use
- Oral contraceptive use
- Magnesium intake
- Caffeine intakes
- Intake of types of fatty acids.

Description of Actual Data Sample:

- *Initial N:* 116,671
- *Attrition (final N):* 91,249
- *Age:* 24 to 44 years at recruitment in 1989
- *Other relevant demographics:* Female nurses
- *Location:* United States.

Summary of Results:

Adjusted[a] Relative Risks (95% Confidence Interval) of Type 2 Diabetes According to Quintiles of Energy-adjusted Glycemic Index, Glycemic Load and Carbohydrate Intake (N=91,249)

Variables	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	P for Trend[b]
Glycemic index	1.00	1.15 (0.90, 1.48)	1.07 (0.83, 1.39)	1.27 (0.98, 1.66)	1.59 (1.21, 2.10)	0.001
Glycemic load	1.00	1.31 (1.05, 1.64)	1.20 (0.92, 1.56)	1.14 (0.84, 1.55)	1.33 (0.92, 1.91)	0.21
Total carbohydrate (% of total energy)	1.00	1.09 (0.87, 1.37)	1.05 (0.80, 1.38)	1.01 (0.74, 1.39)	0.89 (0.60, 1.33)	0.69

[a] Adjusted for age; BMI; energy intake; alcohol intake; physical activity; family history of diabetes; smoking, history of high blood pressure; history of high cholesterol; post-menopausal hormone use; oral contraceptive use; intakes of cereal fiber, magnesium and caffeine; intakes of types of fatty acids.

[b] Based on ordinal variable containing median value for each quintile.

Adjusted[a] Relative Risks (95% Confidence Interval) of Type 2 Diabetes According to Quintiles of Energy-adjusted Fiber Intake (N=91,249)

Variables	Quintile 1	Quintile 2	Quintile 3	Quintile 4	Quintile 5	P for Trend[b]
Total fiber (g per day)	1.00	0.94 (0.76, 1.17)	0.87 (0.68, 1.11)	0.84 (0.65, 1.10)	1.00 (0.75, 1.34)	0.80
Cereal fiber (g per day)	1.00	0.85 (0.69, 1.05)	0.87 (0.69, 1.08)	0.82 (0.65, 1.04)	0.64 (0.48, 0.86)	0.004
Fruit fiber (g per day)	1.00	0.93 (0.75, 1.15)	0.80 (0.63, 1.00)	0.77 (0.60, 0.98)	0.79 (0.60, 1.02)	0.040
Vegetable fiber (g per day)	1.99	0.97 (0.77, 1.22)	1.01 (0.80, 1.28)	1.19 (0.94, 1.51)	1.12 (0.87, 1.46)	0.192

[a] Adjusted for age, BMI, energy intake, alcohol intake, physical activity, family history of diabetes, smoking, history of high blood pressure, history of high cholesterol, post-menopausal hormone use, oral contraceptive use, glycemic load, magnesium intake, caffeine intake; intake of other fiber types (cereal, fruit, vegetable).

[b] Based on ordinal variable containing median value for each quintile.

Key Findings

- GI was significantly associated with an increased risk of type 2 diabetes. Multivariate relative risks for quintiles one to five, respectively, were one, 1.15, 1.07, 1.27, 1.59; 95% CI: 1.21 to 2.10; P=0.001)
- GL was not significantly (NS) associated with risk in the overall cohort.

Other Findings

- The relative risk (RR) for the combination of a high glycemic index and low cereal fiber intake compared with the opposite extreme was 1.75 (95% CI: 1.22, 2.52). P-value for test for interaction between cereal fiber intake and glycemic index was 0.004
- Stratified analysis was conducted to assess effect modification by BMI, physical activity and family history of diabetes. There was no major modification for BMI or for total carbohydrate intake. Among women in the lower two quintiles of activity scores, the multivariate-adjusted relative risks for extreme quintiles were 2.01 (95% CI: 1.38, 2.93) for GI and 1.65 (95% CI: 1.01, 2.70). Among women with no family history of diabetes, the RR across extreme quintiles were 1.02 (95% CI: 0.64, 1.63) for GL and 2.04 (95% CI:1.13, 3.66) for glycemic index. Tests for statistical interaction were NS.

Author Conclusion:

Diets with a high glycemic index and low in cereal fiber increase the risk of type 2 diabetes, particularly in women with a sedentary lifestyle and a family history of diabetes.

Reviewer Comments:

Author-identified potential study limitations:

- *Errors in measurement of dietary intake (limited quantity of available food composition data) may have affected risk estimates*
- *The validity and reliability of the study questionnaire was not tested in the study population, but was assumed based on previous studies in other populations (men and older women).*

Research Design and Implementation Criteria Checklist: Primary Research

Relevance Questions		
1.	Would implementing the studied intervention or procedure (if found successful) result in improved outcomes for the patients/clients/population group? (Not Applicable for some epidemiological studies)	N/A
2.	Did the authors study an outcome (dependent variable) or topic that the patients/clients/population group would care about?	Yes
3.	Is the focus of the intervention or procedure (independent variable) or topic of study a common issue of concern to nutrition or dietetics practice?	Yes
4.	Is the intervention or procedure feasible? (NA for some epidemiological studies)	N/A

Validity Questions		
1.	**Was the research question clearly stated?**	Yes
1.1.	Was (were) the specific intervention(s) or procedure(s) [independent variable(s)] identified?	Yes
1.2.	Was (were) the outcome(s) [dependent variable(s)] clearly indicated?	Yes
1.3.	Were the target population and setting specified?	Yes
2.	**Was the selection of study subjects/patients free from bias?**	Yes
2.1.	Were inclusion/exclusion criteria specified (e.g., risk, point in disease progression, diagnostic or prognosis criteria), and with sufficient detail and without omitting criteria critical to the study?	Yes
2.2.	Were criteria applied equally to all study groups?	Yes
2.3.	Were health, demographics, and other characteristics of subjects described?	Yes
2.4.	Were the subjects/patients a representative sample of the relevant population?	???
3.	**Were study groups comparable?**	Yes
3.1.	Was the method of assigning subjects/patients to groups described and unbiased? (Method of randomization identified if RCT)	N/A

3.2.	Were distribution of disease status, prognostic factors, and other factors (e.g., demographics) similar across study groups at baseline?	N/A
3.3.	Were concurrent controls used? (Concurrent preferred over historical controls.)	N/A
3.4.	If cohort study or cross-sectional study, were groups comparable on important confounding factors and/or were preexisting differences accounted for by using appropriate adjustments in statistical analysis?	Yes
3.5.	If case control or cross-sectional study, were potential confounding factors comparable for cases and controls? (If case series or trial with subjects serving as own control, this criterion is not applicable. Criterion may not be applicable in some cross-sectional studies.)	N/A
3.6.	If diagnostic test, was there an independent blind comparison with an appropriate reference standard (e.g., "gold standard")?	N/A
4.	**Was method of handling withdrawals described?**	Yes
4.1.	Were follow-up methods described and the same for all groups?	Yes
4.2.	Was the number, characteristics of withdrawals (i.e., dropouts, lost to follow up, attrition rate) and/or response rate (cross-sectional studies) described for each group? (Follow up goal for a strong study is 80%.)	N/A
4.3.	Were all enrolled subjects/patients (in the original sample) accounted for?	Yes
4.4.	Were reasons for withdrawals similar across groups?	???
4.5.	If diagnostic test, was decision to perform reference test not dependent on results of test under study?	N/A
5.	**Was blinding used to prevent introduction of bias?**	???
5.1.	In intervention study, were subjects, clinicians/practitioners, and investigators blinded to treatment group, as appropriate?	N/A
5.2.	Were data collectors blinded for outcomes assessment? (If outcome is measured using an objective test, such as a lab value, this criterion is assumed to be met.)	N/A
5.3.	In cohort study or cross-sectional study, were measurements of outcomes and risk factors blinded?	???
5.4.	In case control study, was case definition explicit and case ascertainment not influenced by exposure status?	N/A
5.5.	In diagnostic study, were test results blinded to patient history and other test results?	N/A
6.	**Were intervention/therapeutic regimens/exposure factor or procedure and any comparison(s) described in detail? Were interveningfactors described?**	Yes

6.1.	In RCT or other intervention trial, were protocols described for all regimens studied?	N/A
6.2.	In observational study, were interventions, study settings, and clinicians/provider described?	N/A
6.3.	Was the intensity and duration of the intervention or exposure factor sufficient to produce a meaningful effect?	Yes
6.4.	Was the amount of exposure and, if relevant, subject/patient compliance measured?	Yes
6.5.	Were co-interventions (e.g., ancillary treatments, other therapies) described?	N/A
6.6.	Were extra or unplanned treatments described?	N/A
6.7.	Was the information for 6.4, 6.5, and 6.6 assessed the same way for all groups?	N/A
6.8.	In diagnostic study, were details of test administration and replication sufficient?	N/A
7.	**Were outcomes clearly defined and the measurements valid and reliable?**	Yes
7.1.	Were primary and secondary endpoints described and relevant to the question?	Yes
7.2.	Were nutrition measures appropriate to question and outcomes of concern?	Yes
7.3.	Was the period of follow-up long enough for important outcome(s) to occur?	Yes
7.4.	Were the observations and measurements based on standard, valid, and reliable data collection instruments/tests/procedures?	Yes
7.5.	Was the measurement of effect at an appropriate level of precision?	Yes
7.6.	Were other factors accounted for (measured) that could affect outcomes?	Yes
7.7.	Were the measurements conducted consistently across groups?	Yes
8.	**Was the statistical analysis appropriate for the study design and type of outcome indicators?**	Yes
8.1.	Were statistical analyses adequately described and the results reported appropriately?	Yes
8.2.	Were correct statistical tests used and assumptions of test not violated?	Yes
8.3.	Were statistics reported with levels of significance and/or confidence intervals?	Yes
8.4.	Was "intent to treat" analysis of outcomes done (and as appropriate, was there an analysis of outcomes for those maximally exposed or a dose-response analysis)?	N/A

8.5.	Were adequate adjustments made for effects of confounding factors that might have affected the outcomes (e.g., multivariate analyses)?	Yes
8.6.	Was clinical significance as well as statistical significance reported?	N/A
8.7.	If negative findings, was a power calculation reported to address type 2 error?	N/A
9.	**Are conclusions supported by results with biases and limitations taken into consideration?**	Yes
9.1.	Is there a discussion of findings?	Yes
9.2.	Are biases and study limitations identified and discussed?	Yes
10.	**Is bias due to study's funding or sponsorship unlikely?**	Yes
10.1.	Were sources of funding and investigators' affiliations described?	Yes
10.2.	Was the study free from apparent conflict of interest?	Yes